PERI-IMPLANT SOFT TISSUE AUGMENTATION: CONTRIBUTIONS TO A CONTEMPORARY ISSUE IN IMPLANT DENTISTRY

Summary of the PhD thesis

by

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PUBLICATIONS PROVIDING THE BASIS OF THE THESIS

1. Stähli A*, Párkányi L*, Aroca S, Stavropoulos A, Schwarz F, Sculean A, et al. The effect of connective tissue graft or a collagen matrix on epithelial differentiation around teeth and implants: a preclinical study in minipigs. *Clin Oral Investig* 2023 [epub ahead of print].

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2. Párkányi L, Fráter M. Thickening the attached gingiva around implants - the "H technique" - case presentation [Feszes íny szélesítés implantátumok körül – „H" technika esetismertetés]. *Fogorv Szle* 2018;111(1):12-5.

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ABBREVIATIONS

ASCTG	autogenous subepithelial connective tissue graft
CM/XCM	xenogeneic collagen matrix
SCTG	superficial connective tissue graft
DCTG	deep connective tissue graft
CAF	coronally advanced flap
CDH	clinical defect height
IS	implant shoulder
JE	junctional epithelium

I. INTRODUCTION

The current treatment approaches for the rehabilitation of partially and fully edentulous patients with implant-supported restorations have shown remarkable success and survival rates, even in high-risk populations. By today, dental implantation has been established as a safe and reliable therapeutic approach, and implant-supported restorations offer a significantly higher oral health-related quality of life than their conventional counterparts, especially removable dentures.

Despite the high implant survival rates, implant failure is still a relevant and prevalent problem. Implant failure is commonly attributed to a combination of factors. A growing body of evidence suggests that peri-implant soft tissue augmentation, where applicable, can play a key role in keeping the peri-implant tissues healthy and thus it can lead to higher rates of implant survival. This typically involves grafting, traditionally referring to autogenous connective tissue grafting in this context. Nevertheless, xenogeneic collagen matrices are also being increasingly utilized for this purpose, yielding favorable outcomes. The role of the amount of keratinized tissue and the choice between autogenous subepithelial connective tissue grafts (ASCTGs) and xenogeneic collagen matrices (XCMs) are recurring issues in the recent literature of this topic.

The main clinical indications for soft tissue grafting are recession coverage, keratinized tissue gain, and augmentation of soft tissue volume. Different surgical techniques utilizing different materials have been proposed to achieve soft tissue augmentation in terms of thickness and width, but harvesting of ASCTGs from the palate is still considered as the gold standard. However, despite the well-known benefits of ASCTGs, there are significant drawbacks and limitations associated with this method. These include the morbidity and pain associated with the donor site, which burdens the patient, and the limited availability of donor tissue from the palate, which restricts the number of treatable sites at any given time. To overcome the limitations of ASCTGs, alternative biomaterials have gained importance. Xenogeneic collagen matrices (XCMs) have been proposed as a promising alternative to ASCTGs and have been utilized for soft tissue augmentation around dental implants and root coverage therapy, yielding favorable outcomes. Yet, their use is still a matter of debate, especially because although XCMs have demonstrated good volume stability, their rapid biodegradation caused by enzymatic activity restricts their suitability as a complete replacement for ASCTGs. Another debated aspect is to what extent XCMs can induce keratinization, which appears to be an important factor, despite differing opinions in the literature.

Overall, it seems that for the purposes of peri-implant soft tissue augmentation, xenogeneic collagen matrices will not replace autogenous connective tissue grafting in the foreseeable future. Instead, the two options will coexist, probably with ASCTG still as the standard and XCM as its less invasive alternative, used at the clinician's discretion. Thus, research efforts should still be focused on both approaches, especially that even if ASCTG is the gold standard, several questions remain to be answered in connection with it.

Clinical observations suggest that in many instances, when palatal connective tissue grafts are covered by a non-keratinized mucosal flap, there is a failure of epithelial cell keratinization. These clinical observations align with earlier observations indicating that connective tissue grafts obtained from deeper layers of the palatal connective tissue may not possess the same capacity to induce keratinization as grafts harvested from more superficial layers. However, this remains to be confirmed, as well as the capacity of XCM to induce keratinization. A major part of this thesis deals with these issues.

After tooth loss, during the healing process, the alveolar ridge undergoes varying degrees of resorption, primarily affecting the horizontal dimension. Alveolar involution is not limited to hard tissues alone; it consistently involves a decrease in volume and keratinization in the soft tissues.

Tooth loss, whether due to caries or periodontal reasons, most commonly occurs first in the molar region. The decrease in keratinized tissue is particularly pronounced in the molar region, resulting in a significant absence of it around restorations fixed on molar implants. The molar region is more challenging for patients to access, making it inherently more difficult to clean. In the case of implants, the peri-implant mucosa is more prone to inflammation when exposed to a certain amount of plaque compared to the gingival area adjacent to retained teeth. Thus, soft tissue augmentation in the molar region can be especially important. Acknowledging this and seeking a less invasive solution for a patient requiring molar tooth replacement, we devised the "H-technique," a method for augmenting soft tissue. Subsequently, we discovered its broader applicability in various regions. The latter part of this thesis introduces the said technique and outlines our experiences in implementing it.

II. OBJECTIVES AND HYPOPTHESES

This thesis summarizes two studies, both of which investigated issues related to peri-implant soft tissue augmentation.

The first study examined the differences between superficially (SCTG) and deeply harvested palatal connective tissue grafts (DCTG) and xenogeneic collagen matrices in terms of their impact on epithelial keratinization around teeth and implants that lacked gingiva or keratinized mucosa, respectively. The study was conducted in Göttingen miniature pigs using histological methods. We hypothesized that both superficial and deep connective tissue grafts would induce similar levels of keratinization at teeth and implants. Additionally, we expected that the outcomes achieved with collagen matrices would be comparable to those achieved with connective tissue grafts, without any significant inferiority.

The second study was a proof-of-concept case study exploring an XCM-based surgical technique derived from existing approaches used to manage peri-implant soft tissues, which we call “the H-technique” after the shape of the applied XCM. Conventionally, modifying the biotype and augmenting the thickness or width of the keratinized tissues around implants is performed as a distinct surgical

procedure. This can be carried out either during the uncovering of the implant and placement of the healing abutment or around previously positioned implants with healing abutments. Typically, a free gingival graft is employed for this specific procedure, which may result in considerable donor site morbidity and exhibit aesthetic disparities when compared to the adjacent soft tissues.

The objective of the technique we proposed was to achieve simultaneous modification of the biotype and augmentation of keratinized tissues using XCM during implant placement in an open healing approach. Such a technique is more comfortable for the patient, it eliminates the problem of donor site morbidity, and there is no need for multiple interventions, which shortens net healing time. Beyond these obvious advantages, we hypothesized that by using this technique, enough aesthetic keratinized tissue can be gained to ensure peri-implant soft tissue health even over a longer period.

III. METHODS

III.1. The effects of ASCTG and CTX on epithelial differentiation in minipigs

The study protocol was approved by the local Committee for Animal Research, University of Szeged, Hungary (No. 1-74-2/2015 MAB). Six Göttingen miniature pigs were used for the study. The husbandry and care of the animals before, during, and after surgery was handled at the Surgical Research Unit, University of Szeged, Hungary. The animals received standard food and water ad libitum. Animals were premedicated using ketamine (i.m. 20 mg/kg), xylazine (i.m. 2 mg/kg), atropine (i.v. 0.05 mg/kg) and midazolam (i.v. 0.5 mg/kg) to achieve the intubation status. Inhalation anaesthesia was performed with isoflurane (1.0 - 1.5 %). Fentanyl patches (5 - 10 mg/kg) were used for the intraoperative analgesia and the animals received antibiotic prophylaxis for three days (Duplocillin LA, 12,000 IU/kg).

On one side of the lower jaw, the second, third, and fourth premolars, as well as the first molar, were extracted. Following a healing period of 12 weeks, three 8 - 10 mm long Straumann Standard Plus RN tissue level implants (Straumann, Switzerland) were placed. After an additional 8 weeks of healing, a surgical procedure was performed to create a soft tissue dehiscence around the implants. On the

contralateral side, isolated Miller Class II recession defects were surgically created around the second, third, and fourth premolars. This involved the complete removal of the buccal gingiva, bone, and root cementum using blades, bone chisels, and slowly rotating burs while rinsing with sterile saline, following previously established protocols. The resulting defects had a depth of approximately 5 mm and a width of 4 mm apically to the cemento-enamel junction. The exposed root and implant surfaces were left untreated for 4 weeks to facilitate soft tissue healing, plaque accumulation, and to better simulate a chronic recession-type defect.

After a 4-week healing period, the defects underwent treatment. Initially, the exposed root surfaces of the teeth were thoroughly cleaned using Gracey curettes (Hu-Friedy, Chicago, IL, USA), while the implants received supramucosal cleaning with rubber cups and a polishing paste (Zircate, Prophy Paste; Dentsply, Konstanz, Germany). For teeth, a small bur (diameter 2 mm) was used to mark the most apical part of the previously surgically exposed root surface, creating a reference mark for the histometric analysis. Regarding the implants, clinical defect height (CDH) was measured at the mid-buccal aspect, from the implant shoulder (IS) to the bottom of the mucosal recession. The defects were then treated using a CAF (coronally advanced flap) technique as described by Allen & Miller, along with either a CM

(collagen matrix) or a CTG (connective tissue graft). Two vertical releasing incisions, 6 mm longer than the recession defects, were made. In cases where a CTG was chosen, the required tissue was harvested from the palate, following the technique described by Hürzeler & Weng, with dimensions measuring 0.5 mm less than the size of the vascular bed in mesio-distal length and 5 mm in corono-apical direction. The defects in each quadrant were then randomly assigned to either of the following three treatment groups: CAF + superficial CTG (SCTG) around teeth and implants, or CAF + deep CTG (DCTG) around teeth and implants, or CAF + CM (Mucograft®, Geistlich, Wolhusen, Switzerland) around teeth and implants. The flaps were closed with 6-0 monofil (Polypropylene, Stoma, Emmingen-Liptingen, Germany) suture material. Sutures were removed at 2 weeks. The animals were euthanized after 8 weeks of healing.

The lower jaws were removed and chemically fixed by immersion in 10% buffered formalin supplemented with $CaCl_2$ for 3 weeks. The specimens were rinsed in running tap water, dehydrated in ascending concentrations of alcohol, and embedded in methyl methacrylate, as previously described. Each tooth and implant was sectioned parallel to its longitudinal axis in a bucco-lingual direction, resulting in two to three undecalcified ground sections of ~ 500 µm thickness. The sections were ground to a final thickness of 80 µm, superficially stained with

toluidine blue and basic fuchsin and the two central-most sections were used for descriptive and histomorphometric analyses.

The descriptive analysis was conducted using direct microscopic observation. The sections stained with toluidine blue/fuchsin were examined to assess keratinization/non-keratinization, as well as the presence/absence and extent of inflammation. To provide a basis for comparison, one untreated first molar per animal was used as control. For the histomorphometric analyses, the ground sections were digitized using a Zeiss Axio Imager.M2 microscope (Zeiss, Germany) equipped with an automatic scanning stage and a digital camera. The measurements were carried out on the buccal side of the sections, by the same experienced and calibrated investigator, using the ZEN (Zeiss Efficient Navigation, Zeiss, Germany) software.

III.2. The "H-technique" for the thickening of the attached gingiva around implants

Our middle-aged female patient visited our dental office to have her missing lower left molars (36, 37) replaced.

The patient is a non-smoker, systemically healthy, and maintains excellent oral hygiene. No signs of periodontal disease were detected. However, it was apparent that the bone volume in the implant area and the quantity of soft

tissues were not sufficient. In this case, we encountered a dual challenge as we had to navigate suboptimal conditions for both the hard and soft tissues. Moreover, we aimed to adopt a minimally invasive approach whenever feasible.

Based on CBCT imaging, we planned to place standard-diameter (4.1 mm), short-length (36: 8 mm; 37: 6 mm) Straumann Roxolid implants with screw-retained crown restorations. This approach allowed us to avoid bone grafting and spare the patient from an additional invasive procedure with a relatively long healing period.

For the augmentation of soft tissues, we also aimed to adopt a minimally invasive approach. Therefore, we decided to use a xenogeneic collagen matrix and opted for a minimally invasive surgical technique that we developed as a combination of existing approaches, the "H-technique". The procedure's novelty lay in integrating implantation and augmentation into the same step and the unique application of XCM using an H-shape, which enabled simultaneous thickening of the mucosa (both buccally and lingually) and widening of the keratinized tissue. The applied technique also employed an open wound healing approach, where the healing abutments play a crucial role. The patient has been followed up ever since, the latest follow-up appointment took place in July 2023, 6 years after the procedure.

IV. RESULTS

IV.1. Results from the histologic study[1]

Around both teeth and implants, CAF + SCTG/DCTG/CM resulted in the formation of keratinized epithelium with no differences between SCTG and DCTG. The length of the keratinized epithelium was conspicuously shorter at the experimental teeth compared to the control teeth. All experimental teeth and implants receiving SCTG or DCTG showed pocket formation with subgingival calculus and inflammation, whereas implants receiving CM displayed healthy periimplant soft tissue conditions what implies that CAF + CM was superior to CAF + SCTG/DCTG regarding this aspect. All procedures (CAF + SCTG/DCTG/CM) resulted in a long JE that was even longer at the implants. After 8 weeks of healing, both SCTG and DCTG hardly showed any signs of degeneration or integration into the surrounding tissues.

IV.2. Results from the case study

The sutures were removed two weeks after the surgery. Following this short-term healing, the thickened biotype and initial keratinization were already visible on the

[1] Please note that the study contains an extensive results section, and this section has been shortened to contain only the most important findings. This was necessary to keep the volume of this booklet within reasonable limits. We suggest that the interested reader consult the thesis and the article for details.

exposed collagen matrix surfaces. Upon complete healing (at two months), the thickening of the soft tissues and widening of keratinization in the area were clearly visible, without any discernible differences in color or texture compared to the surrounding tissues, unlike with traditional free gingival graft techniques. Screw-retained fixed dental restorations were placed on the implants, and even after a one-year follow-up, a healthy, stable, and aesthetically pleasing soft tissue profile was observed. This was, of course, greatly influenced by the patient's optimal individual oral hygiene, despite the difficult accessibility of the area. Six years later, in July 2023, the patient returned for a follow-up appointment. During the examination, the patient reported no issues with the implants, prosthetic crowns, or the soft tissues surrounding the implants. The assessment revealed that the soft tissues were in a healthy and aesthetically pleasing condition, closely resembling the state observed six years before.

V. CONCLUSIONS

Through the studies covered in this thesis, we have demonstrated the following and we consider these to be the novel scientific findings related to the work that has been accomplished.

Regarding the histologic study:

- We have demonstrated that after peri-implant soft tissue augmentation with xenogeneic collagen matrix, keratinized tissue is formed. To our knowledge, we are the first to have demonstrated this with histological methods, corroborating widely reported clinical observations.

- All experimental teeth and implants receiving SCTG or DCTG showed pocket formation with subgingival calculus and inflammation, whereas implants treated with XCM displayed healthy peri-implant soft tissue conditions. This suggests that XCM outperformed autogenic SCTG/DCTG in this regard, representing an intriguing new finding that warrants further investigation.

- Contrary to previous suggestions, there was no discernible difference in the ability to induce keratinization between superficial and deep autogenic grafts.

Regarding the clinical case study:

- We have introduced the H-technique, a minimally invasive peri-implant soft tissue augmentation approach.

This innovative technique involves simultaneous implantation and soft tissue augmentation during a single session, utilizing a specially shaped piece of XCM to thicken the mucosa (both buccally and lingually) and widen the keratinized tissue. We have demonstrated that the H-technique can serve as an excellent and less invasive alternative to conventional multistep techniques, offering remarkable short- and long-term results.

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